# Supplementary material:

2	Title:
3	A pilot, open labelled, randomised controlled trial of hypertonic saline nasal irrigation and
4	gargling for the common cold.
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## **Supplementary Methods:**

## INSTRUCTIONS ON THE PREPARATION OF HYPERTONIC SALINE: (FOR VIDEO: WWW.ELVISSTUDY.COM)

### Edinburgh & Lothians Viral Intervention Study

#### Preparation of hypertonic saline:

You are provided two graduated bowls (120ml/250ml) and a flask. You can prepare the solution either in the bowl or in the flask. The instructions are given below.

	o ma	<u>ke 100m</u>	l of 3%	<u>solution</u>	in th	e bowl:
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	Add 3g of sea salt with digital measuring spoon into a clean bowl.
	Add boiled cooled water to 100 ml mark of bowl (warmth – to suit you). If you add freshly
	boiled water instead, wait for it to cool before using.
	Mix to ensure salt dissolves.
	Taste the solution. It should taste salty and NOT too salty or sting your mouth
	☐ If it is too salty or stings your mouth, it will sting your nose.
	☐ If it is too salty, use the highest concentration you are comfortable with.
	☐ See table below for lower concentrations.
	□ Document which concentration you decide to use.
	The table below gives the amount of salt that needs to be added to make solutions of
	different strength or volumes.
To	make larger volumes of hypertonic solution for use during the day:
П	To make a 2% solution, add 15g of soa salt into 500 ml flack provided

- □ To make a 3% solution, add 15g of sea-salt into 500 ml flask provided.
- ☐ Fill the flask to the top with boiling water. Close, shake to mix and then store.
- ☐ Prior to performing HSNIG, pour out required quantity into clean bowl.
- ☐ Wait for it to cool and perform HSNIG.
- ☐ Use a clean flask to prepare solution. Make a fresh batch at least every 24 hours.
- □ Refer to table below to prepare different concentrations. Please document which concentration you decide to use.

#### Table:

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#### Amount of Salt in grams to be added to make different volumes of solution:

	Concentration of solution					
Add g of salt to make solution	3.0%	2.5%	2.0%	1.5%		
100ml – Bowl	3g	2.5g	2g	1.5g		
200ml – Bowl	6g	5g	4g	3g		
500ml – Flask	15g	12.5g	10g	7.5g		

#### How to use the digital measuring spoon:

- ☐ To switch on: Press the "On/Off/Tare" button.
- ☐ Check if it is measuring in **grams**. (If it says Oz, press **"Mode"** to change to **g**).
- ☐ Tare: Press the "On/Off/Tare" button to bring reading to 0.0g
- ☐ Scoop required amount of salt gently.
- ☐ If you need more, scoop required quantity
- ☐ If in excess, gently remove excess.
- ☐ Measure out salt into bowl / flask as appropriate.
- ☐ **To switch off:** Press and hold "On/Off/Tare" button.

#### Caution:

- ☐ Avoid rough handling of the scale. Avoid shaking / dropping scale.
- ☐ Do not use the digital measuring spoon to mix the solution.

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### Edinburgh & Lothians Viral Intervention Study How to perform hypertonic saline nasal irrigation and gargling (HSNIG):

	ose a <b>clean</b> bowl to perform HSNIG.
	Either prepare the solution in a clean bowl or transfer from flask into a clean bowl.
	Wait for solution to cool.
	Bend over the sink, close right nostril.
	Bring bowl to the left nostril such that the solution is in contact with the left nostril.
	Inhale slowly and steadily through the nose. The solution will enter the nose, and go to
	the back of the throat. Do not swallow the solution.
	Some solution will come out via the nose and some via the mouth (keep mouth open).
	Repeat this procedure three times for each nostril.
	If the solution that drains is not clear, repeat the procedure for each nostril until it is clear.
	Then gargle three times with the remainder of the solution.
	Clean the bowl with soap and water and store.
	Blow each nostril gently into a tissue (First with head held straight and next bent over sink
	with chin close to chest to make excess fluid come out. Keeping your chin close to chest
	will assist any liquid which may have entered the sinuses drain).
	For the next 10-15 minutes, you may feel the need to blow your nose a few times.
	After the procedure, your symptoms should decrease. However, symptoms may re-
	appear (within 1-2 hours in the first few days and within 4-5 hours after a few days of
	irrigation). Irrigate as soon as you feel symptoms returning.
	Hence for the first two – three days, you may have to do the procedure for around 6 times
	a day. This should decrease in subsequent days.
	If you wake up in the middle of the night with symptoms, try to perform the procedure as
	it may help you sleep better.

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## Edinburgh & Lothians Viral Intervention Study

### Collecting nasal swabs and return of specimen:

### On day 0: In the presence of the trial nurse.

- o Remove the swab from the packaging
- o Insert the swab into a nostril (left or right) up to the swab's collar.
- o Rotate three times.
- o Insert the swab into the transport medium marked day 0
- Snap the top part of the swab (it will break in the middle where you can see a line).
- o Replace the cap and close the transport medium tight.
- o Hand over the swab to the trial nurse.

#### On days 1-4: At home.

- o The nasal swab has to be collected first thing in the morning.
- Please collect the swab before performing nasal irrigation + gargling if you are in the intervention arm
- o Follow instructions to collect swab as given above
- o On day 1, insert the swab into the transport medium marked day 1
  - On day 2, insert the swab into the transport medium marked day 2
  - $\circ\quad$  On day 3, insert the swab into the transport medium marked day 3
  - o On day 4, insert the swab into the transport medium marked day 4
- Snap the top part of the swab (it will break in the middle where you can see a line).
- $\circ\quad$  Replace the cap and close the transport medium tight.
- Place the sample within a pocket in the absorbent material. Place it in the plastic self-seal bag.
- o Store the sample in a safe place at room temperature.
- On day 4, place all samples in the self-seal plastic bag along with the absorbent material and seal the bag.
- Place the self-seal bag in clear plastic container in the Royal Mail Safebox™(Step 3− Instructions on using the Royal Mail Safebox)
- Remove the card board separator from the lid and dispose of it (Step 5– Instructions on using the Royal Mail Safebox)
- Press the lid over the top of the container and firmly press shut (Step 6– Instructions on using the Royal Mail Safebox)
- Peel the outer backing from the self-adhesive label. Then wrap around the Royal Mail Safebox™ (Step 7/8- Instructions on using the Royal Mail Safebox)
- o Drop of the Royal Mail Safebox™ in any post-box (Step 9– Instructions on using the Royal Mail Safebox).

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Pattern of completion of daily forms: Most participants completed the "WURSS-21-Scot" 26 27 daily until they were well (i.e. a score of 0) on two days. Five individuals completed the daily 28 forms for fourteen days but did not score 0 on two consecutive days. Eleven participants stopped before scoring 0 on 2 consecutive days. Of these, eight scored 0 on the last day of 29 30 completion, two scored 1 on two consecutive days and the last person stopped on day 6 with 31 a score of 5. WURSS-21 and EQ-VAS Scores: From the "WURSS-21-Scot" diaries, the average WURSS-21 32 score could be calculated for each participant over 14 days. Of the 549 "WURSS-21-Scot" 33 diaries, a daily score was not available for 34 records [7=no information, 9 = 0 recorded for 34 35 'how unwell today' and no further questions answered, 18 where questions in the WURSS-21-Scot were missed]. The median (IQR) average WURSS 21 score in the intervention arm was 36 37 13.2 (7.6, 16.4) [n=30] and 16.9 (9.9, 24.7) [n=31] in the control arm (p=0.09). The median average scores and ranges for individual symptoms over 14 days are given in Table S3. Head 38 39 congestion (p=0.04) and sneezing (p=0.03) were significantly lower in the intervention arm. 40 The mean (SD) average quality of life measure (EQ-VAS) over the study duration was higher 41 at 74.3 (12.1) [n=30] for the intervention arm and 70.8 (15.5) [n=31] in the control arm. The 42 difference in means of 3.4, 95% CI for difference (-3.7, 10.6) was not significant (p=0.338). As EQ-VAS, is an indicator of how a person feels on a given day, is not specific to URTI, it is 43 probably not suitable for studies on URTI. 44 45 Change in viral shedding a symptom severity on days after HSNIG was stopped (Intervention 46 arm): Thirteen individuals stopped nasal irrigation before day four followed by an increase in

viral shedding is seen in seven (participants 13-19), and stabilisation of symptoms in eight

- 48 (participant numbers 13-18, 27, 29). Four individuals restarted HSNIG for one or more days
- 49 (participant numbers 5, 17, 27, 29) while in four, symptoms stabilised for 2-3 days before
- 50 becoming asymptomatic (participant numbers 13-16).
- 51 **Difference in viral shedding between arms:** To determine if there was a difference in viral
- 52 shedding between arms, we deducted the baseline value from the end-point sample. A
- 53 negative value means a reduction in viral shedding and a positive value means an increase in
- viral shedding. The median (IQR) reduction in viral shedding in the intervention arm was -2.23
- $\log_{10}$  (-3.04, -0.32) [n=26] and -1.51  $\log_{10}$  (-3.30, -0.55) [n=21] in the control arm. The
- reduction in viral shedding between arms was however not statistically significant (p=0.9).
- 57 Difference in reduction in viral shedding/day between arms: Next the proportion of
- individual with reduction in viral shedding by ≥0.5 log<sub>10</sub>/day was calculated. When all samples
- 59 were included for this calculation, there was no difference between the two arms in the
- proportion of individuals who had a fall ≥0.5 log<sub>10</sub>/day [Intervention arm 65% [n=17/26],
- 61 Control arm 43% [n=9/21], difference -23%, 95% CI for difference in proportion (-50, -5)
- 62 p=0.114]. However, four individuals in the intervention arm had paramyxovirus infection
- (Figure 4; 3=HMPV; 10&21=PIV-3; 25=RSV), but there were no paramyxovirus infections in
- the control arm. Since this could potentially affect the results (as paramyxoviruses tend to
- have a longer life cycle <sup>17,18</sup>, incubation period <sup>19</sup>, duration of viral shedding <sup>20</sup> and illness <sup>20,21</sup>
- compared to rhinovirus <sup>22-25</sup>), we reanalysed the data having removed individuals infected
- 67 with paramyxoviruses. Now, a higher proportion of the intervention arm had a fall ≥0.5
- log<sub>10</sub>/day compared to controls [intervention arm 73% [n=16/22], control arm 43% [n=9/21],
- 69 difference -30%, 95% CI for difference in proportion (-58, -2) p=0.04].

## 71 Table S1: Viruses identified in the day 0 samples.

	Inter	vention	Control	
	(n	=32)	(n:	=34)
	n	%	n	%
Rhinovirus	14	44	13	38
All Coronaviruses (COV)	7	22	8	24
COV-229E	3	9	0	0
COV-OC43	0	0	1	3
COV-HKU1	3	9	5*	15
COV-NL63	1	3	2	6
Enterovirus	2*	6	1**	3
Influenza A virus	1	3	1	3
Respiratory syncytial virus	1	3	1**	3
Parainfluenza virus type 3	2	6	0	0
Human metapneumovirus	1	3	0	0
Negative	5	16	12	35

- 72 The panel included influenza A, B, respiratory syncytial virus, parainfluenza viruses 1-3, rhinovirus,
- enterovirus, parechovirus, COV 229E, COV OC43, COV NL64 and COV HKU1, human metapneumovirus,
- 74 adenovirus, bocavirus and mycoplasma
- 75 \*- 1 dual infection with rhinovirus.
- \*\* No daily forms or follow up samples received.

## 78 Table S2: Days for individual symptoms to get better and functional questions to

## 79 **normalise**:

	Mean da	ays				
Well / Symptoms	Intervention (n=30)	Control (n=31)	Mean Difference	95% C	I Mean	P value
Days to feeling well	6.8	8.7	1.9	0.4	3.3	0.01
Runny nose	6.7	8.5	1.8	0.4	3.2	0.01
Blocked nose	6.0	8.7	2.7	1.2	4.1	<0.001
Sneezing	5.7	7.3	1.5	0.3	2.9	0.02
Sore throat	5.1	6.4	1.3	-0.2	2.8	0.09
Scratchy throat	5.1	6.3	1.2	-0.2	2.5	0.09
Cough	4.9	7.4	2.4	0.9	4.0	0.003
Hoarseness	4.8	6.5	1.7	0.2	3.1	0.02
Head congestion	6.4	7.3	0.9	-0.6	2.4	0.26
Chest congestion	4.4	5.2	0.8	-0.6	2.3	0.25
Feeling tired	6.5	7.9	1.4	0.0	2.8	0.06

## 81 Table S3: Difference in severity of symptoms between arms:

	Intervention (n=30)		Contro	n valva	
	Median	IQR	Median	IQR	p value
Total WURSS-21 score	13.2	7.6, 16.4	16.9	9.9, 24.7	0.09
Runny nose	1.0	0.6, 1.5	1.4	0.8, 2.1	0.21
Blocked nose	0.9	0.4, 1.4	1.4	0.7, 2.2	0.09
Sneezing	0.6	0.4, 0.9	0.9	0.6, 1.5	0.03
Sore throat	0.5	0.1, 0.9	0.6	0.3, 1.4	0.34
Scratchy throat	0.5	0.3, 0.6	0.5	0.1, 1.4	0.94
Cough	0.5	0.1, 1.1	0.9	0.2, 1.9	0.10
Hoarseness	0.3	0.1, 0.8	0.7	0.3, 1.1	0.25
Head congestion	0.7	0.4, 1.1	1.2	0.7, 1.8	0.04
Chest congestion	0.2	0.0, 0.4	0.3	0.0, 1.1	0.33
Feeling Tired	1.0	0.4, 1.4	1.3	0.5, 2.1	0.14
					_
	Mean	SD	Mean	SD	p value
EQ-VAS	74.3	12.1	70.8	15.5	0.338

## Table S4: Feedback about HSNIG – Intervention arm:

		n=28	%
Ease of preparing solution: Easy		28	100
Made solution in bulk (Flask)		24	86
Preferred small bowl for HSNIG		21	75
HSNIG was: Comfortable		11	39
Moderately comfortable		14	50
Uncomfortable		3	11
Performed HSNIG outside home		24	86
If so was it easy to do? Easy		8	29
Moderate		11	39
Difficult		5	18
Equipment cleaning: Easy		27	96
HSNIG on the whole: Convenien	t	11	39
Moderate		14	50
Inconvenie	ent	3	11
Do you feel HSNIG made a difference?	' Yes	26	93
Would you use HSNIG in the future:	Likely	17	61
	Undecided	7	25
	Unlikely	4	14
If HSNIG was more convenient:	Likely	24	86
	Undecided	2	7
	Unlikely	2	7
Would you use HSNIG for prophylaxis:	Likely	6	21
	Undecided	2	7
	Unlikely	20	71

## **Supplementary figures:**

# Figure S1: Daily Form "WURSS-21-Scot"

Edinburgh a	ind Loth	iians \	∕iral	Inter	vent	ion Stu	ıdy	Edinburgh and Lothians Viral Intervention Study Edinburgh and Lothians Viral Intervention Stud
Subject Number:			Date:		Time	e:		Subject Number: Date: Time: Subject Number: Date: Time:
	Dai	ly Form	ı – Da	y 1				Daily Form – Day 1 Daily Form – Day 1
	Not unwel	1	2	Mildly 3	4	Moderately 5	Severe	7 S.d. Frieder Finder you and a minuted to either blow or not blow your nose before hasai 20. wagana wagana san sa
1 How unwell do you feel today     Once you have answered 'no'     not need to complete any fur     study form'.      Please rate the average se	t unwell' for rther informa	tion on tl	he daily	form. Pl	ease go	num of 14 c directly to	the 'End of	O Did you collect nasal swab? Yes O No O To help people say how good or bad a health state of the people say how good or bad a health s
symptom	Do not have this	Very Mil	dly 2	Mildly 3	4	Moderately 5	Severel	How much salt have you used?, grams opinion. Please do this by drawing a line from the
Runny nose	0	0	0	0	0	0	0 0	
Blocked (plugged) nose	0	0	0	0	0	0	0 0	indicates how good or bad your health state is
Sneezing	0	0	0	0	0	0	0 0	6. How many times have you performed the procedure in the last 24 hours? today.
Sore throat	0	0	0	0	0	0	0 0	5 0 10 20 30 40 50 60 70 80 90 110 110 120
Scratchy throat	0	0	0	0	0	0	0 0	5
Cough	0	0	0	0	0	0	0 0	7. What techniques did you use? Irrigation + gargle O health state
Hoarseness	0	0	0	0	0	0	0 0	O Irrigation only O today
Head congestion	0	0	0	0	0	0	0 0	O Gargle only O
Chest congestion	0	0	0	0	0	0	0 0	O None O
Feeling tired	0	0	0	0	0	0	0 0	O If none please indicate reason:
3. Over the last 24 hours, ho	w much has y	your cold	interfe	red with	your abi	lity to:		***************************************
	Not at all	Very Mile	dly	Mildly		Moderately	Sever	erety 8. Did you notice any side effects? Yes O No O
	0	1	2	3	4		6 7	
Think clearly	0	0	0	0	0		0 0	ii yes please indicate now severe you let these.
Sleep well	0	0	0	0	0		0 0	TVOIC SEVELE
Breathe easily	0	0	0	0	0		0 0	11. Since you last completed these questions have you sought further medical
Walk, climb stairs, exercise	0	0	0	0	0		0 0	attention for your cold?
Accomplish daily activities	0	0	0	0	0	_	0 0	Yes O No O
Work outside the home	0	0	0	0	0	_	0 0	- Tall
Work inside the home	0	0	0	0	0	_	0 0	if yes where did you seek help?
Interact with others	0	0	0	0	0		0 0	Trumy nose 0 0 0 0 0 0 0
Live your personal life	0	0	0	0	0	0	0 0	O Other O O O O O Hospital O
4. Compared to yesterda	ıy, I feel that	my cold is	s:					If other please describe: Other O please specify:
Very much Somewhat	A little			A little	Son	newhat V	ery much	<u> </u>
better better	better	The sa	me	worse	W	orse	worse	9. Since you last completed these questions have you taken any cold / flu related (If you have answered Yes to this question, please go to the "End of study form"
0 0	0	0		0		0	0	9. Since you last comprete times questions have you caken any cold / no related medications? Yes O No O
								If yes, what did you take?
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## Figure S2: End-of-Study Form

### Edinburgh and Lothians Viral Intervention Study

#### **End of Study Form** Subject Number: Time: 1. As a result of your symptoms did you: No 🗌 Take any time off work/education?: If yes please indicate number of days: days Take any medications? No 🗌 If yes please provide details: Visit your GP Attend hospital No 2. Did anyone else in your house experience similar symptoms after you? Yes No If yes, how many adults experienced symptoms How many children experienced symptoms 3. Did you perform gargling/nasal irrigation: Yes If no please go to question 6, if yes please complete the following: If you were allocated to the control arm, i.e. not allocated to perform nasal irrigation / gargling, what method did you use and how did you find out about this method? If you were allocated to the intervention arm. Which container did you usually make up the solution in? Small bowl Large bowl Which bowl did you usually use to perform gargling/irrigation? Small bowl Large bowl Please select the box that best describes the following statements: Very Moderate Difficult easy How comfortable was the procedure? How easy was it to make the solution? How easy was it to perform outside your home? How easy was it to clean everything required for the procedure? How easy was it to carry with you everything required for the procedure? How convenient did you find the procedure as a whole?

### Edinburgh and Lothians Viral Intervention Study

4. Do you feel the procedure has made a difference to your symptoms?

If yes, what difference do you feel it has	made:	Υe	_	No			
							- - -
5. Future use of gargling/nasal irriga		lowina st	atemeni	ls.			
Trease select the box that beet describe	0 010 101	Ve like	y is		lecided	Unlikely	Very
If you have the symptoms of the cold in			1				
how likely would you be to use this proc If the procedure was more convenient how likely would you be to use this proc	to perfor	m, _	] [	3			
Would you consider perform gargling/irrigation procedure once or to as a preventative measure?		he ay □	] [	<b>-</b>			
6. Study procedures and documenta Please select the box that best describe		lowing st	atemeni	ts:			
	Did not perform	Very easy	Easy	Mod	erate	Difficult	Very
How easy was it for you to collect the swabs?				[			
How easy was it to return the swabs?				[			
How easy was it to complete the daily diary information?							
How easy was it to complete the other forms?				[			
	Not viewed	Very helpful	Helpful	Unde	cided	Unhelpful	Very
How helpful did you find the information provided before joining the				[			
STUDV							
study? How helpful did you find the instructions and information provided in your study pack?				[			

ELVIS End of Study form V1.0, 26/10/2014